Thereby certify that this correspondence is deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Commissioner for Patents, Washington, XC 20231" on

UC No. 2000-0007 UC No. B02-016 PATENT

25 MARZOOZ

signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Jay KEASLING et al.

Serial No.: 10/006,909

Filing Date: December 6, 2001

Group Art Unit: 1645

Examiner: Unassigned

Title: BIOSYNTHESIS OF ISOPENTENYL PYROPHOSPHATE

### Information Disclosure Statement

Commissioner for Patents Washington, DC 20231

Sir:

This is an Information Disclosure Statement submitted for the Examiner's consideration. Applicants respectfully request that the Examiner review and make of record the references identified below.

A PTO-1449 form listing the references accompanies this paper. Applicants would appreciate the Examiner's initialing and returning the form to indicate that the references have been reviewed and made of record. The references are as follows:

	U.S. PATENT DOCUMENTS	
Document No.	Issue Date or Publication Date	Name of Patentee or Applicant
6,072,045	6/6/00	Chappell et al.
6,114,160	9/5/00	Croteau et al.
6,190,895	2/20/01	Croteau et al.
6,281,017	8/28/01	Croteau et al.
6,284,506	9/4/01	Hoshino et al.
6,291,745	9/18/01	Meyer et al.
6,306,633	10/23/01	Wilding et al.

#### NONPATENT DOCUMENTS

Altincicek et al. (2001), "GcpE Is Involved in the 2-C-Methyl-D-Erythritol 4-Phosphate Pathway of Isoprenoid Biosynthesis in *Escherichia coli*," *Journal of Bacteriology* 183(8):2411-2416.

Amann et al. (1988), "Tightly Regulated *Tac* Promoter Vectors Useful for the Expression of Unfused and Fused Proteins in *Escherichia coli*," *Gene* 69:301-315.

Barkovich et al. (2001), "Metabolic Engineering of Isoprenoids," Metabolic Engineering 3(1):27-39.

Campos et al. (2001), "Identification of *gcpE* as a Novel Gene of the 2-*C*-Methyl-D-Erythritol 4-Phosphate Pathway for Isoprenoid Biosynthesis in *Escherichia coli*," *FEBS Letters* <u>488</u>:170-173.

Atty Dkt No. 2000-0007 Serial No. 10/006,909

This Information Disclosure Statement is not intended as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any of the above references constitutes prior art to the present application within the meaning of 35 USC § 102.

As applicants have not yet received a first Action on the merits, no fee is required for filing this Information Disclosure Statement. If, however, the PTO finds that for some reason a fee is found to be necessary, our Deposit Account No. 18-0580 may be charged therefor. A duplicate copy of this paper is enclosed.

Respectfully submitted,

By:

Mark A. Wilson

Registration No. 43,275

REED & ASSOCIATES 800 Menlo Avenue, Suite 210 Menlo Park, California 94025 (605) 330-0900 Telephone (650) 330-0980 Facsimile



Atty Dkt No. 2000-0007 Serial No. 10/006,909

#### NONPATENT DOCUMENTS

Campos et al. (2001), "Escherichia coli Engineered to Synthesize Isopentenyl Diphosphate and Dimethylallyl Diphosphate from Mevalonate: A Novel System for the Genetic Analysis of the 2-C-Methyl-D-Erythritol 4-Phosphate Pathway for Isoprenoid Biosynthesis," *Biochem. J.* 353:59-67.

Cunningham et al. (1994), "Molecular Structure and Enzymatic Function of Lycopene Cyclase from the Cyanobacterium *Synechococcus* sp Strain PCC7942," *The Plant Cell* 6:1107-1121.

Dairi et al. (2001), "Eubacterial Diterpene Cyclase Genes Essential for Production of the Isoprenoid Antibiotic Terpentecin," *Journal of Bacteriology* 183(20):6085-6094.

Guzman et al. (1995), "Tight Regulation, Modulation, and High-Level Expression by Vectors Containing the Arabinose P<sub>BAD</sub> Promoter," *Journal of Bacteriology* 177(14):4121-4130.

Hahn et al. (1999), "Escherichia coli Open Reading Frame 696 Is idi, a Nonessential Gene Encoding Isopentenyl Diphosphate Isomerase," Journal of Bacteriology 181(15):4499-4504.

Hahn et al. (2001), "1-Deoxy-D-Xylulose 5-Phosphate Synthase, the Gene Product of Open Reading Frame (ORF) 2816 and ORF 2895 in *Rhodobacter capsulatus*," *Journal of Bacteriology* 183(1):1-11.

Hamano et al. (2001), "Cloning of a Gene Cluster Encoding Enzymes Responsible for the Mevalonate Pathway from a Terpenoid-Antibiotic-Producing Streptomyces Strain," Biosci. Biotechnol. Biochem. 65(7):1627-1635.

Kaneda et al. (2001), "An Unusual Isopentenyl Diphosphate Isomerase Found in the Mevalonate Pathway Gene Cluster from *Streptomyces* sp. Strain CL190," *PNAS* 98(3):932-937.

Kim et al. (2001), "Metabolic Engineering of the Nonmevalonate Isopentenyl Diphosphate Synthesis Pathway in *Escherichia coli* Enhances Lycopene Production," *Biotechnology and Bioengineering* 72(4):408-415.

Kovach et al. (1994), "pBBR1MCS: A Broad-Host-Range Cloning Vector," BioTechniques 16(5):800-802.

Kovach et al. (1995), "Four New Derivatives of the Broad-Host-Range Cloning Vector pBBR1MCS, Carrying Different Antibiotic-Resistance Cassettes," *Gene* 166:175-176.

Mahmoud et al. (2001), "Metabolic Engineering of Essential Oil Yield and Composition in Mint by Altering Expression of Deoxyxylulose Phosphate Reductoisomerase and Menthofuran Synthase," *PNAS* 98(15):8915-8920.

McAteer et al. (2001), "The *lytB* Gene of *Escherichia coli* Is Essential and Specifies a Product Needed for Isoprenoid Biosynthesis," *Journal of Bacteriology* 183(24):7403-7407.

Oulmouden et al. (1991), "Nucleotide Sequence of the *ERG12* Gene of *Saccharomyces cerevisiae* Encoding Mevalonate Kinase," *Current Genetics* 19:9-14.

Polakowski et al. (1998), "Overexpression of a Cytosolic Hydroxymethylglutaryl-CoA Reductase Leads to Squalene Accumulation in Yeast," *Appl. Microbiol. Biotechnol.* 49:66-71.

Rohdich et al. (2002), "Studies on the Nonmevalonate Terpene Biosynthetic Pathway: Metabolic Role of IspH (LytB) Protein," *PNAS* 99(3):1158-1163.

Rohlin et al. (2001), "Microbioal Pathway Engineering for Industrial Processes: Evolution, Combinatorial Biosynthesis and Rational Design," *Current Opinion in Microbiology* 4:330-335.

Rohmer et al. (1993), "Isoprenoid Biosynthesis in Bacteria: A Novel Pathway for the Early Steps Leading to Isopentenyl Diphosphate," *Biochem. J.* 295:517-524.

Sandmann (2001), "Carotenoid Biosynthesis and Biotechnological Application," *Archives of Biochemistry and Biophysics* 385(1):4-12.

Szkopinska et al. (2000), "The Regulation of Activity of Main Mevalonic Acid Pathway Enzymes: Farnesyl Diphosphate Synthase, 3-Hydroxy-3-Methylglutaryl-CoA Reductase, and Squalene Synthase in Yeast Saccharomyces cerevidiae," Biochemical and Biophysical Research Communications 267:473-477.

Takagi et al. (2000), "A Gene Cluster for the Mevalonate Pathway from *Streptomyces* sp. Strain CL190," *Journal of Bacteriology* 182(15):4153-4157.

Toth et al. (1996), "Molecular Cloning and Expression of the cDNAs Encoding Human and Yeast Mevalonate Pyrophosphate Decarboxylase," *The Journal of Biological Chemistry* 271(14)7895-7898.

Tsay et al. (1991), "Cloning and Characterization of *ERG8*, an Essential Gene of *Saccharomyces cervisiae* that Encodes Phosphomevalonate Kinase," *Molecular and Cellular Biology* 11(2):620-631.

Wang et al. (1999), "Engineered Isoprenoid Pathway Enhances Astaxanthin Production in *Escherichia coli*," *Biotechnology and Bioengineering* 62(2):235-241.

Wang et al. (2000), "Directed Evolution of Matabolically Engineered Escherichia coli for Carotenoid Production," *Biotechnol. Prog.* 16(6):922-926.

substitute	tim	form	1 1 10	A /DTO	

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	2

Con Lete if Known				
Application Number	10/006,909			
Filing Date December 6, 2001				
First Named Inventor	Jay KEASLING et al.			
Art Unit	1645			
Examiner Name	Unassigned			
Attorney Docket Number	2000-0007			

	U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No.	Document No.	Issue Date or Publication Date	Name of Patentee or Applicant of Cited Document	Class	Subclass	Filing Date if Appropriate
	AA	6,072,045	6/6/00	Chappell et al.			
	AB	6,114,160	9/5/00	Croteau et al.			
	AC	6,190,895	2/20/01	Croteau et al.			
	AD	6,281,017	8/28/01	Croteau et al.			
	AĒ	6,284,506	9/4/01	Hoshino et al.			
	AF	6,291,745	9/18/01	Meyer et al.			
	AG	6,306,633	10/23/01	Wilding et al.			

		OTHER DOCUMENTS — NONPATENT LITERATURE DOCUMENTS	
Examiner	Cite	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate). Title of the item (book, magazine,	Т
Initials*	No.	journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Ļ
	AΗ	Altincicek et al. (2001), "GcpE Is Involved in the 2-C-Methyl-D-Erythritol 4-Phosphate Pathway of	
_		Isoprenoid Biosynthesis in Escherichia coli," Journal of Bacteriology <u>183</u> (8):2411-2416.	$oldsymbol{ol}}}}}}}}}}}}}}}}}}$
	ΑI	Amann et al. (1988), "Tightly Regulated <i>Tac</i> Promoter Vectors Useful for the Expression of Unfused and	
		Fused Proteins in <i>Escherichia coli</i> ," <i>Gene</i> <u>69</u> :301-315.	
	ΑJ	Barkovich et al. (2001), "Metabolic Engineering of Isoprenoids," <i>Metabolic Engineering</i> 3(1):27-39.	
	AK	Campos et al. (2001), "Identification of gcpE as a Novel Gene of the 2-C-Methyl-D-Erythritol 4-Phosphate	
		Pathway for Isoprenoid Biosynthesis in <i>Escherichia coli</i> ," <i>FEBS Letters</i> 488:170-173.	
	AL	Campos et al. (2001), "Escherichia coli Engineered to Synthesize Isopentenyl Diphosphate and	
		Dimethylallyl Diphosphate from Mevalonate: A Novel System for the Genetic Analysis of the 2-C-	
		Methyl-D-Erythritol 4-Phosphate Pathway for Isoprenoid Biosynthesis," <i>Biochem. J.</i> 353:59-67.	
	AM	Cunningham et al. (1994), "Molecular Structure and Enzymatic Function of Lycopene Cyclase from the	T
		Cyanobacterium Synechococcus sp Strain PCC7942," The Plant Cell 6:1107-1121.	
	AN	Dairi et al. (2001), "Eubacterial Diterpene Cyclase Genes Essential for Production of the Isoprenoid	1
		Antibiotic Terpentecin," Journal of Bacteriology 183(20):6085-6094.	
	AO	Guzman et al. (1995), "Tight Regulation, Modulation, and High-Level Expression by Vectors Containing	$\vdash$
	710	the Arabinose P <sub>BAD</sub> Promoter," <i>Journal of Bacteriology</i> 177(14):4121-4130.	
	AP	Hahn et al. (1999), "Escherichia coli Open Reading Frame 696 Is idi, a Nonessential Gene Encoding	1
	711	Isopentenyl Diphosphate Isomerase," <i>Journal of Bacteriology</i> 181(15):4499-4504.	
	AQ	Hahn et al. (2001), "1-Deoxy-D-Xylulose 5-Phosphate Synthase, the Gene Product of Open Reading	╁
	ΛŲ	Frame (ORF) 2816 and ORF 2895 in <i>Rhodobacter capsulatus</i> ," <i>Journal of Bacteriology</i> 183(1):1-11.	
	AR	Hamano et al. (2001), "Cloning of a Gene Cluster Encoding Enzymes Responsible for the Mevalonate	$\vdash$
	AK	Pathway from a Terpenoid-Antibiotic-Producing Streptomyces Strain," Biosci. Biotechnol. Biochem.	
		, , , , , , , , , , , , , , , , , , ,	
		65(7):1627-1635.	-
	AS	Kaneda et al. (2001), "An Unusual Isopentenyl Diphosphate Isomerase Found in the Mevalonate Pathway	
		Gene Cluster from Streptomyces sp. Strain CL190," PNAS 98(3):932-937.	_
	ΑT	Kim et al. (2001), "Metabolic Engineering of the Nonmevalonate Isopentenyl Diphosphate Synthesis	
		Pathway in Escherichia coli Enhances Lycopene Production," Biotechnology and Bioengineering	
		<u>72</u> (4):408-415.	
	ΑU	Kovach et al. (1994), "pBBR1MCS: A Broad-Host-Range Cloning Vector," <i>BioTechniques</i> 16(5):800-	
		802.	
	AV	Kovach et al. (1995), "Four New Derivatives of the Broad-Host-Range Cloning Vector pBBR1MCS,	
		Carrying Different Antibiotic-Resistance Cassettes," <i>Gene</i> 166:175-176.	

Examiner	Date	
Signature	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute	for	form	1449A/PTC

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	2	of	2

Concrete if Known				
Application Number	10/006,909			
Filing Date	December 6, 2001			
First Named Inventor	Jay KEASLING et al.			
Art Unit	1645			
Examiner Name	Unassigned			
Attorney Docket Number	2000-0007			

	OTHER DOCUMENTS — NONPATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate). Title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Т			
	AW	Mahmoud et al. (2001), "Metabolic Engineering of Essential Oil Yield and Composition in Mint by				
		Altering Expression of Deoxyxylulose Phosphate Reductoisomerase and Menthofuran Synthase," <i>PNAS</i> 98(15):8915-8920.				
	AX	McAteer et al. (2001), "The <i>lytB</i> Gene of <i>Escherichia coli</i> Is Essential and Specifies a Product Needed for Isoprenoid Biosynthesis," <i>Journal of Bacteriology</i> 183(24):7403-7407.				
	AY	Oulmouden et al. (1991), "Nucleotide Sequence of the <i>ERG12</i> Gene of <i>Saccharomyces cerevisiae</i> Encoding Mevalonate Kinase," <i>Current Genetics</i> 19:9-14.				
_	AZ	Polakowski et al. (1998), "Overexpression of a Cytosolic Hydroxymethylglutaryl-CoA Reductase Leads to Squalene Accumulation in Yeast," <i>Appl. Microbiol. Biotechnol.</i> 49:66-71.				
	BA	Rohdich et al. (2002), "Studies on the Nonmevalonate Terpene Biosynthetic Pathway: Metabolic Role of IspH (LytB) Protein," <i>PNAS</i> 99(3):1158-1163.				
	BB	Rohlin et al. (2001), "Microbioal Pathway Engineering for Industrial Processes: Evolution, Combinatorial Biosynthesis and Rational Design," <i>Current Opinion in Microbiology</i> 4:330-335.				
	BC	Rohmer et al. (1993), "Isoprenoid Biosynthesis in Bacteria: A Novel Pathway for the Early Steps Leading to Isopentenyl Diphosphate," <i>Biochem. J.</i> 295:517-524.				
	BD	Sandmann (2001), "Carotenoid Biosynthesis and Biotechnological Application," <i>Archives of Biochemistry and Biophysics</i> 385(1):4-12.				
	BE	Szkopinska et al. (2000), "The Regulation of Activity of Main Mevalonic Acid Pathway Enzymes: Farnesyl Diphosphate Synthase, 3-Hydroxy-3-Methylglutaryl-CoA Reductase, and Squalene Synthase in Yeast Saccharomyces cerevidiae," Biochemical and Biophysical Research Communications 267:473-477.				
	BF	Takagi et al. (2000), "A Gene Cluster for the Mevalonate Pathway from <i>Streptomyces</i> sp. Strain CL190," <i>Journal of Bacteriology</i> 182(15):4153-4157.				
	BG	Toth et al. (1996), "Molecular Cloning and Expression of the cDNAs Encoding Human and Yeast Mevalonate Pyrophosphate Decarboxylase," <i>The Journal of Biological Chemistry</i> : 271(14)7895-7898.				
	ВН	Tsay et al. (1991), "Cloning and Characterization of <i>ERG8</i> , an Essential Gene of <i>Saccharomyces cervisiae</i> that Encodes Phosphomevalonate Kinase," <i>Molecular and Cellular Biology</i> 11(2):620-631.				
	BI	Wang et al. (1999), "Engineered Isoprenoid Pathway Enhances Astaxanthin Production in <i>Escherichia coli</i> ," <i>Biotechnology and Bioengineering</i> 62(2):235-241.				
	BJ	Wang et al. (2000), "Directed Evolution of Matabolically Engineered Escherichia coli for Carotenoid Production," <i>Biotechnol. Prog.</i> <u>16</u> (6):922-926.				

Examiner	Date	
Signature	 Considered	